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EXAMINER	
LEESER, ERICH A	
ART UNIT	**PAPER NUMBER**
1624	

SHORTENED STATUTORY PERIOD OF RESPONSE	NOTIFICATION DATE	DELIVERY MODE
3 MONTHS	04/04/2007	ELECTRONIC

Please find below and/or attached an Office communication concerning this application or proceeding.

If NO period for reply is specified above, the maximum statutory period will apply and will expire 6 MONTHS from the mailing date of this communication.

Notice of this Office communication was sent electronically on the above-indicated "Notification Date" and has a shortened statutory period for reply of 3 MONTHS from 04/04/2007.

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PTO-PAT-Email@rfem.com

Office Action Summary	Application No.	Applicant(s)	
	10/510,626	CARCELLER GONZALEZ ET AL.	
	Examiner	Art Unit	
	Erich A. Leeser	1624	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *08 October 2004*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *38-74* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *38-74* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☒ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *April 21, 2005*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Priority

1. Acknowledgment is made that this application is a 371 of PCT/EP03/03635, filed on April 8, 2003, which claims foreign priority to application SPAIN 2002 00805, filed on April 8, 2002.

Information Disclosure Statement

2. The references cited in the IDS, dated April 21, 2005, are made of record.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

3. Claims 38-74 are rejected under 35 U.S.C. 112, first paragraph, because the specification does not reasonably provide enablement for making a "prodrug" of the claimed compounds. The claim(s) contain subject matter that is not described in the specification in such a way as to enable one skilled in the art of medicinal chemistry to make and use the invention.

4. In evaluating the enablement question, several factors are to be considered. 1) The nature of the invention, 2) the state of the prior art, 3) the predictability or lack thereof in the art, 4) the amount of direction or guidance present, 5) the presence or absence of working examples, 6) the breadth of the claims, and 7) the quantity of experimentation needed. *In re Wands*, 858 F.2d 731, 8 USPQ2d 1400 (Fed. Cir. 1988).

The nature of the invention

5. Heterocyclic amides with alpha-4 integrin antagonist activity, including prodrugs thereof.

The state of the prior art:

6. The state of the prodrug art is summarized by Wolff, Manfred E., *Burger's Medicinal Chemistry and Drug Discovery*, Fifth Ed., Vol. 1: Principles and Practice, John Wiley & Sons, 1995, 975. The table on the left side of page 976 outlines the research program to be undertaken to find a prodrug. The second paragraph in section 10 and the paragraph spanning pages 976-977 indicate the low expectation of success. In that paragraph the difficulties of extrapolating between species are further developed. Since the prodrug concept is a pharmacokinetic issue, the lack of any standard pharmacokinetic protocol discussed in the last sentence of this paragraph is particularly relevant. Banker, Gilbert S. et al., *Modem Pharmaceutics*, Marcel Dekker, New York, 1996, in the first sentence, third paragraph on page 596 states that "extensive development must be undertaken" to find a prodrug.

The predictability or lack thereof in the art:

7. It is well-established that "the scope of enablement varies inversely to the degree of unpredictability of the factors involved", "and physiological activity is generally considered to be an unpredictable factor." *In re Fisher*, 427 F.2d 833, 839, 166 USPQ 18, 24 (CCPA 1970). Finding a prodrug is an empirical exercise. Predicting if a certain ester of a claimed alcohol, for example, is in fact a prodrug, and produces the active compound metabolically, in man, at a therapeutic concentration and at a useful rate, is filled with experimental uncertainty. Although attempts have been made to predict drug metabolism *de novo*, this is still an experimental science. For a compound to be a prodrug, it must meet three tests. First, the prodrug must itself

be biologically inactive. Second, the prodrug must be metabolized to a second substance in a human at a rate and to an extent to produce that second substance at a physiologically meaningful concentration. Thirdly, that second substance must be biologically active.

The amount of direction or guidance present:

8. The amount of guidance or direction refers to that information in the application that teaches exactly how to make or use the invention. The specification contains no working examples of a prodrug of a compound of the formula I. Thus, undue experimentation will be required by one skilled in the art to make the prodrugs of the claimed invention.

The presence or absence of working examples:

9. The specification contains no working examples of a prodrug of a compound of the formula I. Thus, undue experimentation will be required to determine if any particular derivative is, in fact, a prodrug.

The breadth of the claims:

10. The breadth of the claims includes all of the hundreds of thousands of compounds of claim 1 as well as the presently unknown list of potential prodrug derivatives embraced by the word "prodrug." The term is important in claim 1 because claims are to be given their broadest reasonable interpretation that is consistent with the specification. Because the specification does not adequately teach one skilled in the chemical arts how to sufficiently make the claimed prodrugs of the present invention without undue experimentation, the scope of the claims is broader than the scope of the specification. It would not be obvious to one skilled in the art how to make the prodrugs of the present invention. Therefore, the scope of enablement provided to

one skilled in the art by the disclosure is not commensurate with the scope of protection sought by the claims.

The quantity of experimentation needed

11. Substantial and undue experimentation would be needed to practice Applicant's invention because he did not sufficiently detail how to make and use a "prodrug" of the instant invention. MPEP 2164.01(a) states, "A conclusion of lack of enablement means that, based on the evidence regarding each of the above factors, the specification, at the time the application was filed, would not have taught one skilled in the art how to make and/or use the full scope of the claimed invention without undue experimentation. *In re Wright*, 999 F.2d 1557,1562, 27 USPQ2d 1510, 1513 (Fed. Cir. 1993)." That conclusion is clearly justified here.

12. In view of the seven factors, *supra*, one having ordinary skill in the art would have to undergo an undue amount of experimentation to make and use the instantly claimed invention.

13. Claims 38-74 are rejected under 35 U.S.C. 112, first paragraph, because the specification does not reasonably provide enablement for making solvates of the claimed invention. The specification does not enable a person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

In evaluating the enablement question, several factors are to be considered. 1) The nature of the invention, 2) the state of the prior art, 3) the predictability or lack thereof in the art, 4) the amount of direction or guidance present, 5) the presence or absence of working examples, 6) the breadth of the claims, and 7) the quantity of experimentation needed. *In re Wands*, 858 F.2d 731, 8 USPQ2d 1400 (Fed. Cir. 1988).

The nature of the invention:

14. The invention is drawn to compounds of formula I (and processes for making and methods for using same), "or a salt, solvate or prodrug thereof." The specification is not adequately enabled to show how to make solvates of compounds of formula I. The specification on page 24 recites: "Some compounds of the present invention can exist in solvated form, including hydrated forms. In general, the solvated forms, with pharmaceutically acceptable solvents such as water, ethanol and the like, are equivalent to the unsolvated form for the purposes of the invention," but there is no enablement of such compounds.

15. The compounds of formula I embrace heterocyclic amides with alpha-4 integrin antagonist activity substituted with variable groups R^1 to R^8, W, Z, E, X, A, L, B, m, n, p, Cy, Het^1, Het^2 and R^a to R^h.

16. Even a cursory calculation of the number of compounds embraced in the instant formula I would result in perhaps thousands of compounds. This is of course far more compounds than the specification enables one skilled in the art to make. Thus, the genus embraced in claim 38 is too large and there is no teaching of any solvate of this large genus.

The state of the prior art:

17. A search in the pertinent art, including water as solvent resulted in a pertinent reference, is indicative of the unpredictability of solvate formation in general. The state of the art is that it is not predictable whether solvates will form or what their composition will be. In the language of the physical chemist, a solvate of an organic molecule is an interstitial solid solution. This phrase is defined in the second paragraph of West, Anthony R., *Solid State Chemistry and Its Applications*, Wiley, New York, 1988, 358. The solvent molecule is a species introduced into

the crystal and no part of the organic host molecule is left out or replaced. In the first paragraph: "it is not usually possible to predict whether solid solutions will form, or if they do form what is the compositional extent". West, Anthony R., *Solid State Chemistry and Its Applications*, Wiley, New York, 1988, 365. Thus, in the absence of undue experimentation one cannot predict if a particular solvent will solvate any particular crystal. One cannot predict the stoichiometry of the formed solvate, i.e. if one, two, or a half a molecule of solvent is added per molecule of host.

The predictability or lack thereof in the art:

18. For the reasons stated *supra*, the solvates as applied to the above-mentioned compounds claimed by the Applicant are not art-recognized compounds and hence there should be an enabling disclosure in the specification with working example(s).

The amount of direction or guidance present:

19. Examples illustrated in the experimental section are limited to making the compounds not related to solvates. There is no example of solvates of the instant compounds. A multiplicity of compounds were shown in the examples of the specification each of which come in contact with a solvent but there is no showing that the instant compounds formed solvates. Hence it is clear that merely bringing the compounds in contact with solvent does not result in solvate and additional direction or guidance is needed on how to make them. The specification has no such direction or guidance.

The presence or absence of working examples:

20. There is no working example of any solvate formed. These cannot be simply willed into existence. "The specification purports to teach, with over fifty examples, the preparation of the claimed compounds with the required connectivity. However ... there, is no evidence that such

compounds exist... the examples of the '881 patent do not produce the postulated compounds... there is ...' no evidence that such compounds even exist." *Morton Int'l Inc. v. Cardinal Chem. Co.*, 5 F.3d 1464, 28 USPQ2d 1190 (1993). The same circumstance appears to be true here. There is no evidence that solvates of these compounds actually exist; if they did, they would have formed. Hence, there should be a showing of supporting evidence that solvates of these compounds exist and therefore can be made.

The breadth of the claims:

21. The breadth of the claims include all of the perhaps thousands of compounds of formula I of claim 38 as well as the presently unknown list of potential solvate derivatives embraced by these terms. The term is important in claim 38 because claims are to be given their broadest reasonable interpretation that is consistent with the specification. Because the specification does not adequately teach one skilled in the chemical arts how to sufficiently make the claimed solvates of the present invention without undue experimentation, the scope of the claims is broader than the scope of the specification. It would not be obvious to one skilled in the art how to make the solvates of the present invention. Therefore, the scope of enablement provided to one skilled in the art by the disclosure is not commensurate with the scope of protection sought by the claims.

The quantity of experimentation needed

22. The specification has insufficient support, as noted *supra*, for the desired solvates of the compounds of formula I. As noted above, the genus embraces perhaps thousands of compounds and hence the breadth of the claims is broad. The quantity of experimentation needed would be an undue burden on one skilled in the chemical art since there is inadequate guidance given to

the skilled artisan for the many reasons stated *supra*. Even with the undue burden of experimentation, there is no guarantee that one would get the product of desired solvates of the compounds of formula I embraced in the instant claims.

23. In view of the seven factors, *supra*, one having ordinary skill in the art would have to undergo an undue amount of experimentation to use the instantly claimed invention commensurate in scope with the claims.

24. Claims 63-66 and 70-74 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement because while being enabling for the treatment of asthma, allergic rhinitis, allergic dermatitis, allergic conjunctivitis, rheumatoid arthritis, psoriatic arthritis, multiple sclerosis, psoriasis, diabetes, Crohn's disease and ulcerative colitis, the specification does not enable the instant compounds to (1) treat *all* diseases in some way connected to alpha-4 integrin antagonist activity, including all inflammatory diseases, immune diseases, autoimmune diseases, degenerative disorders, tumor metastasis and ischemia-reperfusion disorders using a compound of formula 1 or enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

25. There are many factors to be considered when determining whether there is sufficient evidence to support a determination that a disclosure does not satisfy the enablement requirement and whether any necessary experimentation is "undue." These factors include 1) the breadth of the claims, 2) the nature of the invention, 3) the state of the prior art, 4) the level of one of ordinary skill, 5) the level of predictability in the art, 6) the amount of direction provided by the inventor, 7) the existence of working examples, and 8) the quantity of experimentation needed to

make or use the invention based on the content of the disclosure. *In re Wands*, 858 F.2d 731, 737, 8 USPQ2d 1400, 1404 (Fed. Cir. 1988).

The nature of the invention:

26. The instant invention is drawn to heterocyclic amides with alpha-4 integrin antagonist activity, including methods of treating inflammatory diseases, immune diseases, autoimmune diseases, degenerative disorders, tumor metastasis and ischemia-reperfusion disorders using a compound of formula 1.

The state of the prior art:

27. The prior art at the time the invention was made at times points towards enablement of some of Applicant's method claims, "[t]he accumulation of leukocytes in various organs contributes to the pathogenesis of a number of human autoimmune diseases such as asthma, rheumatoid arthritis, Chohn's disease, ulcerative colitis, hepatitis C, and multiple sclerosis; but at the same time points away from enablement of Applicant's broader method claims, "[w]hether [alpha-4] integrin antagonists will eventually become a new class of organ-selective anti-inflammatory agents, remains unclear." Jackson, D., *Alpha 4 Integrin Antagonists*, Current Pharmaceutical Design, 2002, 8, 1229-1253.

The predictability in the art:

28. It is noted that the pharmaceutical art is unpredictable, requiring each embodiment to be individually assessed for physiological activity. *In re Fisher*, 427 F. 2d 833, 166 USPQ 18 (CCPA 1970) indicates that the more unpredictable an area is, the more specific enablement is necessary in order to satisfy the statute. In the instant case, the claimed invention is highly unpredictable since one skilled in the art would not necessarily recognize, with regards to

therapeutic effects, whether or not the compounds of formula I would be useful for treating *all* inflammatory diseases, immune diseases, autoimmune diseases, degenerative disorders, tumor metastasis and ischemia-reperfusion disorders.

Amount of guidance/working examples:

29. The only example in the specification showing the activity of various alpha-4 integrin antagonists is found on pages 50-53 of the specification. The included table; however, does not definitely prove that the instant compounds can be used for treating all inflammatory diseases, immune diseases, autoimmune diseases, degenerative disorders, tumor metastasis and ischemia-reperfusion disorders using a compound of formula 1 to a subject in need thereof.

The breadth of the claims:

30. The instant invention is drawn to methods of treating inflammatory diseases, immune diseases, autoimmune diseases, degenerative disorders, tumor metastasis and ischemia-reperfusion disorders using a compound of formula I to a subject in need thereof.

The quantity of undue experimentation needed:

31. Since the guidance and teaching provided by the specification is insufficient for treating all inflammatory diseases, immune diseases, autoimmune diseases, degenerative disorders, tumor metastasis and ischemia-reperfusion disorders using a compound of formula I to a subject in need thereof, one of ordinary skill in the art, even with a high level of skill, is unable to practice the invention as claimed without undue experimentation.

The level of the skill in the art:

32. The level of skill in the art is high. Due to the unpredictability in the pharmaceutical art; however, it is noted that each embodiment of the invention is required to be individually assessed

for physiological activity by *in vitro* and *in vivo* screening to determine which compounds exhibit the desired pharmacological activity and which diseases or diseases would benefit from this activity.

33. Taking all of the above factors into consideration, it is not seen how one of ordinary skill in the art would be able to make and use the compounds of formula I for treating inflammatory diseases, immune diseases, autoimmune diseases, degenerative disorders, tumor metastasis and ischemia-reperfusion disorders using a compound of formula I to a subject in need thereof without undue experimentation.

34. Claims 63-74 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for treating specific diseases, see *supra*, does not reasonably provide enablement for *preventing* diseases. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to use the invention commensurate in scope with these claims. Applicants are not enabled for preventing any of these diseases. The only established prophylactics are vaccines not the alpha-4 antagonist compounds such as present here. In addition, it is presumed that "prevention" of the claimed diseases would require a method of identifying those individuals who will develop the claimed diseases before they exhibit symptoms. There is no evidence of record that would guide the skilled clinician to identify those who have the potential of becoming afflicted.

35. "The factors to be considered [in making an enablement rejection] have been summarized as the quantity of experimentation necessary, the amount of direction or guidance presented, the presence or absence of working examples, the nature of the invention, the state of the prior art,

the relative skill of those in that art, the predictability or unpredictability of the art, and the breadth of the claims", *In re Rainer*, 146 USPQ 218 (1965); *In re Colianni*, 195 USPQ 150, *Ex parte Formal*, 230 USPQ 546. 1) As discussed above, preventing diseases requires identifying those patients who will acquire the disease before administration of a compound of formula I could occur. This would require extensive and potentially open-ended clinical research on healthy subjects. 2) Appicant intends to treat inflammatory diseases, immune diseases, autoimmune diseases, degenerative disorders, tumor metastasis and ischemia-reperfusion disorders using a compound of formula I to a subject in need thereof. 3) There is no working example of such a preventive procedure in man or animal in the specification. 4) The claims rejected are drawn to organic chemistry and are therefore physiological in nature. 5) The state of the art is that no general procedure is art-recognized for determining which patients generally will become infected before the fact. 6) The artisan using Applicants invention would be a Board Certified physician in pathology with an MD degree and several years of experience. Despite intensive efforts, pharmaceutical science has been unable to find a way of getting a compound to be effective for the prevention of inflammatory diseases, immune diseases, autoimmune diseases, degenerative disorders, tumor metastasis and ischemia-reperfusion disorders generally. Under such circumstances, it is proper for the PTO to require evidence that such an unprecedented feat has actually been accomplished, *In re Ferens*, 163 USPQ 609. No such evidence has been presented in this case. The failure of skilled scientists to achieve a goal is substantial evidence that achieving such a goal is beyond the skill of practitioners in that art, *Genentech vs. Novo Nordisk*, 42 USPQ2nd 1001, 1006. This establishes that it is not reasonable to any agent to be able to prevent inflammatory diseases, immune diseases, autoimmune

diseases, degenerative disorders, tumor metastasis and ischemia-reperfusion disorders generally. That is, the skill is so low that no compound effective generally against inflammatory diseases, immune diseases, autoimmune diseases, degenerative disorders, tumor metastasis and ischemia-reperfusion disorders has ever been found let alone one that can prevent such conditions. 7) It is well established that "the scope of enablement varies inversely with the degree of unpredictability of the factors involved", and physiological activity is generally considered to be an unpredictable factor. See *In re Fisher*, 427 F.2d 833, 839, 166 USPQ 18, 24 (CCPA 1970). 8) The claims broadly read on all patients, not just those undergoing therapy for the claimed diseases and on the multitude of compounds embraced by formula I.

36. The Examiner suggests deletion of the word "prevention".

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

37. Claims 38-74 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which Applicant regards as the invention. The following apply. Any claim not specifically rejected is rejected if it is dependent on a rejected claim and shares the same indefiniteness.

38. Recitation of "prodrug" in claim 38 renders claim 38 and its dependent claims 39-74 indefinite. Prodrugs, in general, are compounds, which undergo *in vivo* hydrolysis to parent active drugs. In that sense recitation of prodrug is acceptable. However, it is not clear what the difference is between these variable groups and the prodrug groups. There is clear-cut ambiguity as to what is to be considered a prodrug and what is not. Applicants should note that if the

variable groups are prodrug, which are in general inactive but becomes active upon *in vivo* transformation, then the compound bearing the variable group would be deemed as inactive, which is not what the claim recites.

39. Furthermore, the issue of the second paragraph of 35 U.S.C § 112 is whether the structures of the claimed compounds are clearly defined. Applicants' "prodrug" are molecules whose structure lie outside the subject matter, but upon metabolism in the body are converted to active compounds falling within the structural scope of the instant claims. The claim describes the function intended but provides no specific structural guidance as to what constitutes a "prodrug." Structural formulas, names, or both can accurately describe organic compounds, which are the subject matter of the instant claims. Attempting to define means by function is not proper when the means can be clearly expressed in terms that are more precise.

40. Throughout claim 38 it currently reads "can be optionally substituted with one or more groups." This claim language is indefinite because it is unclear whether the optional substituents are a claim limitation or not. As such, "can be" should be replaced with "is" to obviate this rejection.

41. Claim 61 is rejected because step (k) states that, "a compound of formula I [is transformed] into another compound of formula I." This is indefinite because it is not clear why one skilled in the art would need to transform one compound of formula I (the end product) into another compound of formula I as it seems unnecessary and inefficient. More importantly, this step is indefinite because the language does not inform the reader *which* compound of formula I is transformed into *which* new compound of formula I. Clarification is suggested to obviate this rejection.

42. Claim 63 is rejected because it uses the indefinite term, "mediated." This claim language is indefinite because it renders the scope of the claim indefinite.

Conclusion

Any inquiry concerning this communication or earlier communications from the Examiner should be directed to Erich A. Leeser whose telephone number is 571-272-9932. The Examiner can normally be reached Monday through Friday from 8:30 to 6:00 EST.

If attempts to reach the Examiner by telephone are unsuccessful, the Examiner's supervisor, Mr. James O. Wilson can be reached at 571-272-0661. The fax number for the organization where this application is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) toll-free at 866-217-9197. If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

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